REMARKS

I. Status of the Claims

Claims 1-30 were filed with the application, are under examination, and stand rejected under 35 U.S.C. §112, first paragraph, 35 U.S.C. §112, second paragraph, 35 U.S.C. §102 and 35 U.S.C. §103. The specific grounds for rejection, and applicants' response thereto, are set out in detail below.

II. Objections to the Specification and Claims

The drawings stand objected to under MPEP §608.02(d). Replacement Sheets for the drawings are attached and should show structural detail as described in the specification.

Claim 29 is objected to as depending on itself. An appropriate amendment is provided.

III. Rejection Under 35 U.S.C. §112, First Paragraph

Claims 1-30 stand rejected under §112, first paragraph as lacking an enabling disclosure. Applicants traverse.

In contrast to the examiner's argument, the rejection is not based on a balanced weighing of the eight enumerated *Wands* factors – to the contrary, it is based on disbelief that applicants' methods will work. Indeed, the examiner even admits that the data presented in applicants' specification shows "the role and importance of endothelial cells during ***successful islet transplantation***." Office Action at page 5 (emphasis added). And importantly, the examiner acknowledges that there was a showing of islet cell survival, insulin production and vascularization, involving both donor and host endothelial cells, and that about 40% of the revascularization derives from donor cells. This is *prima facie* evidence of enablement, and the

examiner has admitted such. The ***only*** rebuttal of these data is that the "optimal" number of endothelial cells and insulin-producing cells is not provided. Optimization is not required to "make and use" the claimed invention according to §112, first paragraph – only objective enablement is required.

The examiner goes on to challenges the breadth of "insulin-producing" cells in applicants' claims. However, it is not argued that a wide variety of cells cannot be engineered to make insulin, just that there are hurdles to fully exploiting such resources. In point of fact, Yamaoka (2002) provides a "favorable" outlook on such endeavors. Indeed, the other cited references indicate "effective" preventive methods and instead critique "*in vivo*" targeting of vectors, which is not claimed here. Thus, again, the objective evidence to support the examiner's challenge is missing from the record.

In sum, the rejection is based on disbelief, not on a credible challenge stemming from the scientific community. Moreover, enablement does not require clinical success, but instead, a valid scientific basis for the claimed invention. That is provided here by applicants' data. In light of this showing, reconsideration and withdrawal of the rejection is respectfully requested.

IV. Rejections Under 35 U.S.C. §112, Second Paragraph

Claims 1, 4, 5, 21, 24 and 25 are rejected as indefinite over use of the term "quality." Applicants traverse, but in the interest of advancing the prosecution, the claims have been amended to remove that term.

Claims 8 and 10 are rejected as indefinite over use of the term "distinct living donor." Applicants traverse, but in the interest of advancing the prosecution, the claims have been amended to remove that term.

Reconsideration and withdrawal of the rejection are respectfully requested.

V. Rejection Under 35 U.S.C. §102

Claims 1-4, 7, 8, 10-12, 21-24 and 26 stand rejected as anticipated by U.S. Patent Publication 2003/0113302A1. Applicants traverse.

The title of the cited publication is "Use of ***reciplent*** endothelial cells for enhanced vascularization of tissue and tissue-engineered construct transplants" (emphasis added). This constitutes a teaching away from the present invention, which relies on ***donor*** endothelial cells for revascularization. The examiner clearly recognizes this, but argues that there is "inherent" anticipation due to the handling of cells according to the publication. Interestingly, though every other citation to the publication is supported by a specific paragraph or claim, no support is provided for a teaching of culturing to improve the quality of the endothelial cells in the transplant. As such, the rejections is facially defective.

More importantly, in order for an "inherent disclosure" to anticipate a claimed invention, ***the inherency must be certain***. *Ex parte McQueen*, 123 USPQ 37 (Bd. App. 1958). Here, the examiner is merely guessing that an improvement in quality is achieved. Thus, it is submitted that this is precisely the situation which the *McQueen* Board sought to address when it stated that the inherency must be certain. Furthermore, applicants note that inherency cannot be based on a prior art process when those of skill in the art did not realize the result of the process. *In re Marshall*, 198 USPQ 344 (CCPA 1978); *In re Fenton*, 179 USPQ 295 (CCPA 1973). This constitutes yet another reason why the rejection cannot stand.

Reconsideration and withdrawal of the rejection are respectfully requested.

VI. Rejections Under 35 U.S.C. §103

A. '302 Publication in view of Osborne *et al.*, Nagarajan *et al.*, Kalka *et al.* and Ryan *et al.*

Claims 1-4, 6-18, 21-24, 26 and 27 are rejected as obvious over the '302 Publication in view of Osborne *et al.*, Nagarajan *et al.*, Kalka *et al.* and Ryan *et al.* Applicants traverse. As explained above, it has not been established that the method of the '302 publication inherently provides the benefits of applicant's methods, namely, improving the quantity and/or quality of endothelial cells from the transplant. The secondary references do not cure this defect – indeed, the examiner does not even argue as much, relying instead on the illusory teachings of the '302 publication. The misapplication of the inherency doctrine is even more notable here, in the context of obviousness, which is based on ***what those of skill in the art would apprehend from the cited references***. It is black letter law that "The inherency of an advantage and its obviousness are entirely different questions. That which may be inherent is not necessarily known. ***Obviousness cannot be predicated on what is unknown.***" *In re Spormann*, 150 USPQ 449 (CCPA 1966) (emphasis added). Reconsideration and withdrawal of the rejection are respectfully requested.

B. '302 Publication in view of Rhim *et al.*, Takahashi *et al.* and Bilbano *et al.*

Claims 21 and 28-30 are rejected as obvious over the '302 Publication in view of Rhim *et al.*, Takahashi *et al.* and Bilbano *et al.* Applicants traverse. As explained above, it has not been established that the method of the '302 publication inherently provides the benefits of applicant's methods, namely, improving the quantity and/or quality of endothelial cells from the transplant.

The secondary references do not cure this defect – indeed, the examiner does not even argue as much, relying instead on the illusory teachings of the '302 publication. The misapplication of the inherency doctrine is even more notable here, in the context of obviousness, which is based on ***what those of skill in the art would apprehend from the cited references***. It is black letter law that "The inherency of an advantage and its obviousness are entirely different questions. That which may be inherent is not necessarily known. ***Obviousness cannot be predicated on what is unknown.***" *In re Spormann*, 150 USPQ 449 (CCPA 1966) (emphasis added). Reconsideration and withdrawal of the rejection are respectfully requested.

VII. Conclusion

In light of the foregoing applicants respectfully submit that all claims are in condition for allowance, and an early notification to that effect is earnestly solicited. Should the examiner have any questions regarding this submission, a telephone call to the undersigned at the number below is invited.

Applicants respectfully request that the enclosed postcard be date-stamped and returned as evidence or receipt.

Respectfully submitted,

Reg. #57,423
for

Steven L. Highlander
Reg. No. 37,642
Attorney for Applicants

FULBRIGHT & JAWORSKI L.L.P.
600 Congress Avenue, Suite 2400
Austin, Texas 78701
(512) 474-5201

Date: April 20, 2006